Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (Canceled)

2. (Canceled)

3. (Currently amended) The method of claim 40, wherein the retention layer [[is]] ~~composed of~~ comprises a particulate material.

4. (Original) The method of claim 3, wherein the retention layer consists of glass beads.

5. (Currently amended) The method of claim 40, wherein the retention layer [[is]] ~~composed of~~ comprises a rigid retention material.

6. (Currently amended) The method of claim 5, wherein the rigid retention material comprises sinter plates.

7. (Currently amended) The method of claim 40, wherein the clarification reactor has a top and a bottom, wherein the retention layer is disposed inside the clarification reactor between the top and the bottom of the clarification reactor,

wherein the mixture comprising the precipitate and the lysate enters the top of the clarification reactor, and the lysate exits the bottom of the clarification reactor, with the precipitate being retained within the clarification reactor by the retention layer,

wherein in step d), increasing pressure is applied at the top of the clarification reactor to the mixture comprising the precipitate and the lysate ~~from the top of the clarification reactor~~, thereby ensuring a constant outflow of the lysate from the bottom of the clarification reactor.

8. (Previously Presented) The method of claim 7, wherein pressure is increased by applying pressurized air.

9. (Previously Presented) The method of claim 40, wherein one or more wash steps are inserted between steps d) and e).

10. (Canceled)

11. (Currently amended) The method of claim 40, wherein the flow of the cell suspension and the flow of the ~~alkaline~~ lysis solution are combined, without further mixing, before entering the lysis reactor, thus forming a single flow within the lysis reactor that is thoroughly mixed when flowing through the particulate material in the lysis reactor.

12. (Previously Presented) The method of claim 40, wherein the cell suspension and the lysis solution are introduced into the lysis reactor in the form of two independent flows.

13. (Currently amended) The method of claim 12, wherein [[said]] the two flows are introduced from independent sources through T-type or Y-type connectors, thus forming a single flow.

14. (Currently amended) The method of claim 12 or 13, wherein [[said]] the two flows are transported at a defined ratio of flow rates, thereby ensuring a constant ratio of cell suspension and lysis solution volumes.

15. (Currently amended) The method of claim 40, wherein in step c), the lysed cell solution obtained in step b) is mixed with ~~a neutralizing~~ the neutralization solution in a continuous mode.

16. (Currently amended) The method of claim 15, wherein the lysed cell solution and the ~~neutralizing~~ neutralization solution are combined at a constant ratio of flow rates.

17. (Previously Presented) The method of claim 40, wherein a concentration and/or a conditioning step is inserted between step d) and step e).

18. (Previously Presented) The method of claim 17, wherein a concentration step and a condition step are inserted, and wherein said concentration step takes place before said conditioning step.

19. (Previously Presented) The method of claim 40, wherein said biomolecule of interest is a polynucleotide.

20. (Previously Presented) The method of claim 19, wherein the polynucleotide is plasmid DNA.

Claims 21 and 22. (Canceled)

23. (Previously Presented) The method of claim 40 wherein, in addition, step a) is operated in a continuous mode.

24. (Currently amended) The method of claim 40, wherein the cell suspension obtained in step a) is ~~host cells obtained in step a) are~~ cryo-pelleted.

Claims 25 – 39 (Canceled)

40. (Currently amended) A method of ~~producing~~ purifying a biomolecule of interest from a host cell using an automated or semi-automated device comprising:

a) cultivating host cells to produce the biomolecule of interest and forming a cell suspension of the cultivated host cells, wherein the cell suspension is a fermentation broth containing the cultivated host cells or a re-suspension of the cultivated host cells that are harvested from the fermentation broth; ~~and optionally harvesting and re-suspending the cultivated host cells;~~

b) introducing the cell suspension and [[the]] a lysis solution into a lysis reactor at a defined ratio of flow rates and disintegrating the cultivated host cells by alkaline lysis in the ~~an alkaline~~ lysis reactor to produce a lysed cell solution, wherein the lysis reactor contains ~~containing~~ a particulate material;

c) neutralizing, in a neutralization reactor, the lysed cell solution to produce a mixture comprising a ~~alkaline~~ lysate and ~~precipitating~~ a precipitate comprising cellular debris and impurities, wherein the lysate contains the biomolecule of interest, and wherein the neutralization reactor is fluidly connected to the ~~akaline~~ lysis reactor and the lysed cell solution ~~lysis solution~~ is mixed with [[the]] a neutralization solution in [[a]] the neutralization reactor;

d) separating, in a clarification reactor, ~~neutralized~~ the lysate containing the biomolecule of interest from the precipitate ~~precipitated cellular debris and impurities~~, wherein the neutralization reactor is fluidly connected to the clarification reactor so that the mixture comprising the precipitate and the lysate is allowed ~~and allows the lysate~~ to flow through the clarification reactor, wherein

the clarification reactor contains ~~containing~~ a retention layer that ~~material, and said retention material~~ functions to separate the precipitate from the lysate so that the precipitate is retained by the retention layer and the lysate is allowed to ~~retain the precipitate on top and within the retention material while allowing the purified lysate~~ to flow from the clarification reactor; and

e) purifying the biomolecule of interest, where the biomolecule of interest is purified from the lysate that flows from the clarification reactor,

wherein said method is operated on a manufacturing scale.

41. (Currently amended) The method of ~~Claim~~ claim 40, wherein one or more distribution means are disposed inside the clarification reactor and extend to a surface of the retention layer, wherein the one or more distribution means ~~are employed to reach the surface of the retention layer and~~ evenly distribute [[a]] the mixture [[of]] comprising the precipitate and the lysate as obtained in step c) into the clarification reactor of step d).

42. (New) The method of claim 40, wherein the particulate material consists of glass beads.

43. (New) The method of claim 7, wherein the retention layer has a top facing the top of the clarification reactor and a bottom facing the bottom of the clarification reactor, wherein the retention layer functions to retain the precipitate on the top of and within the

retention material while allowing the purified lysate to flow from the clarification reactor.

44. (New) The method of claim 40, wherein the lysis reactor is essentially completely filled with the particulate material.